28. A method for treating a subject having diarrhoea comprising administering to the subject an effective amount of a composition comprising a peptide according to ~~claim~~ 27.

REMARKS

Claims 1 to 11 were pending in this application in its published PCT format. Claims 2 to 5 and 8 to 11 were cancelled without prejudice, claims 6 and 7, amended, and claims 12 to 28 have been added. The changes were made to conform the set to U.S. practice, replacing use claims with method claims, and to streamline the case and save considerable fees by re-writing multiple dependent claims as dependent claims. As amended, the application has a standard U.S. set of twenty claims (1, 7, 8, and 12 to 28), three of which are independent (1, 13, and 27).

The specification was amended to add the abstract found on page 1 of the published PCT application, and the sequence listing section of that application was replaced with one that conforms to U.S. practice, changing the single letter amino acid abbreviations to three-letter designations, presenting bases in lower case, adding as SEQ ID NO 6 a control peptide mentioned in the Examples on page 45, and adding information identifying the listing. No new matter is presented.

Newly presented claim 12 tracks the language of formerly presented claim 8, listing diseases that can be found in the specification on page 32 at lines 21 to 2 and on page 39 in item 16. New claim 13 particualarly points out useful peptides of the invention set out in SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, and SEQ ID NO 5, and their homologues and variants, as described on page 16 at lines 11 to 12 and page 37 at lines 24 to 26 of the specification. Claim 14 is directed to peptides of the invention having from about 5 to about 40 amino acids; support for the limitation can be found in the specification on page 14 at line 31. New claims 15 to 18 particularly point out homologues of the peptides described on page 15 at lines 6 to 8 and 11 to 12 and on page 16, line 22. New claim 19 tracks the language of claim 6 and is supported in the specification on page 38 at lines 16 to 17. Claim 20 particularly points out compositions comprising a peptide

of the invention and an agent that binds specifically to the β4-α2 loop of EtxB or CtxB as set out in the specification on page 39 in item 11. In many embodiments, the agent is an antibody as particularly pointed out in claim 21; support for this added limitation may be found in the specification on page 39 in item 12. Claims 22 to 25 particularly point out that peptides of the invention are especially useful for a variety of pathological states characterized by diarrhoea such as cholera or enterotoxin-mediated diarrhoeal disease as described in the specification on page 8, lines 18 to 19. Claim 26 particularly points out that the invention encompasses the treatment of toxin-mediated disorders described in the specification on page 8 at lines 19 to 20. New claims 27 and 28 particularly point out a preferred embodiment that is an isolated fragment of the β4-α2 loop of EtxB/CtxB and comprises the sequence shown in SEQ ID NO 2 or a sequence exhibiting 85% homology to SEQ ID NO 2; support for the limitations may be found in the specification on page 8 at lines 18 to 19, on page 14 at lines 25 to 26, and on page 16 at line 22. No new matter is presented.

The claimed invention provides new peptide fragments of cholera toxin B or enterotoxin B for use primarily as vaccine adjuvants, but also for the treatment and prevention of a variety of diseases including autoimmune disease, human T cell leukaemia, transplant rejection or graft-versus-host disease, allergies, and infectious diseases, particularly for diarrhoea (both cholera and enterotoxin-mediated diarrhoeal disease). Applicants request early and favorable consideration of the claims.

If the undersigned can advance the prosecution of this application in any way, the Examiner is invited to call at the number listed below.

Respectfully submitted,

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<u>Version With Markings to Show Changes Made</u>

6 (Original). A substance according to claim 1 ~~any one of the preceding claims~~ wherein the substance additionally comprises an antigen or an antigenic determinant.

7 (Original). A pharmaceutical composition comprising the substance according to claim 1 ~~any one of claims 1 to 6~~, optionally admixed with one or more pharmaceutically acceptable carrier(s), diluent(s) or excipient(s).